REMARKS

Applicants respectfully request entry of the foregoing, re-examination and reconsideration of the subject matter identified in caption, as amended, pursuant to and consistent with 37 C.F.R. §1.116, and in light of the remarks which follow.

Claims 1, 3-10 and 12-21 are pending in the application, claims 2 and 11 having been canceled above and new claims 19-21 having been added above.

By the above amendments, claim 2 is canceled and claim 1 is amended to include the subject matter of canceled claim 2. Claim 11 is canceled and claim 10 is amended to include the subject matter of canceled claim 11. Claim 10 is further amended to read in part, "... said composition comprising an amount of at least one agent sufficient to elicit an irritant side effect to a user when utilized in a composition that does not include an interleukin 1 antagonist or a TNF-alpha antagonist and wherein said irritant agent is an active agent in said composition. Claim 10 is further amended in this manner to be consistent with the amendment to claim 1 and the accompanying remarks provided in the Amendment filed on December 20, 2001, to obviate the §112 rejection for use of the phrase "one agent which produces an irritant side-effect." Finally, new claims 19-21 have been added to further define preferred embodiments of the invention. Support for claims 19-21 can be found at least at claim 1 of the original application.

Applicants thank Examiners Padmonabhan and Wells for the courtesies extended to their representative during the personal interview of September 17, 2002. In this regard, the Examiners' Interview Summary accurately describes the substance of the interview.

Turning now to the Official Action, claims 1-18 stand rejected under the judicially created doctrine of double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,658,581 and over claims 15-41 of U.S. Patent No. 6,060,061. As agreed during the personal interview, because the present application is a divisional of co-pending application 09/391,399, which is a continuation of U.S. Patent No. 5,993,833, which is a divisional of U.S. Patent No. 5,658,581, a terminal disclaimer is not required to obviate the rejection over the '581 patent. In order to obviate the rejection over the '061 patent, Applicants have filed the enclosed terminal disclaimer.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1 and 10-11 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In view of the above amendments and the issues discussed during the personal interview, Applicants submit that these rejections are moot.

Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-2, 5-8, 10-11 and 14-17 stand rejected under 35 U.S.C. §102(b) as being unpatentable over *Parker* (U.S. Patent No. 5,039,695). For at least the reasons that follow, withdrawal of the rejection is in order.

The present invention relates to the use of a histamine antagonist, an interleukin-1 antagonist and/or a TNF-alpha antagonist in a cosmetic, pharmaceutical or dermatological composition for topical application, intended, in particular, for the treatment of sensitive skin, as well as to a composition containing a histamine antagonist, an interleukin-1

antagonist and/or a TNF-alpha antagonist for the purpose of decreasing or even abolishing the irritant effects of certain products, and in particular of certain active agents used in the cosmetics, pharmaceutical or dermatological field. See specification at page 1, paragraph 2.

For example, independent claim 1, as amended above, sets forth a composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition, an amount of at least one compound selected from the group consisting of interleukin-1 antagonists, TNF-alpha antagonists and combinations thereof, sufficient to prevent or alleviate said irritant side-effect, and a cosmetically, dermatologically or pharmaceutically acceptable medium therefor wherein the agent which elicits the irritant side-effect is selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts,antimetabolites, vitamin D and depigmentation agents.

It is well established that in order to demonstrate anticipation under §102(b), each element of the claim in issue must be found, either expressly described or under principles of inherency, in a single prior art reference. See *Kalman v. Kimberly-Clark Corp.*, 218 U.S.P.Q. 789 (Fed. Cir. 1983). That is not the case here.

Parker relates to certain aryl- and heteroaryl-alkyl-pyrrole carboxylic acid compounds of the formula I and to salts thereof. Additionally, *Parker* is related to the

pharmacological use of the compounds of formula I as interleukin-1 inhibitors effective in alleviating interleukin-1 mediated conditions. See *Parker* at column 1, line 55 to column 2, line 9.

Parker does not disclose or suggest each feature of the presently claimed invention. For example, *Parker* does not disclose or fairly suggest a composition comprising an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts,antimetabolites, vitamin D and depigmentation agents as set forth, for example, in independent claims 1 and 100.

For at least these reasons, Applicants submit that the presently claimed invention is not anticipated by *Parker*. Accordingly, reconsideration and withdrawal of the rejection are in order.

Claims 1-18 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Parker* in view of *Blank* (U.S. Patent No. 5,605,894). For at least the reasons that follow, withdrawal of the rejection is in order.

For at least all of the reasons set forth above, Applicants submit that the presently claimed invention also would not have been obvious over *Parker*.

Further, Applicants submit that *Blank* does not generate the deficiencies of *Parker*. That is, *Blank* does not disclose or suggest a composition comprising an irritant agent that

is an active agent in the composition and is selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts,antimetabolites, vitamin D and depigmentation agents to arrive at the presently claimed invention.

For at least these reasons, Applicants submit that the presently claimed invention would not have been obvious over *Parker* in view of *Blank*. Accordingly, reconsideration and withdrawal of the rejection are in order.

Claims 1-18 stand rejected under 35 U.S.C. §103(a) as being unpatentable over *Blank* in view of *Skotniki* (U.S. Patent No. 4,902,800). For at least the reasons that follow, withdrawal of the rejection is in order.

For at least all of the reasons set forth above, Applicants submit that the combination of *Blank* in view of *Skotniki* also would not have rendered obvious the presently claimed invention. That is, the presently claimed invention would not have been obvious over the asserted combination because the asserted combination fails to disclose or fairly sugest a composition comprising an irritant agent that is an active agent in the composition, the agent being selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts,antimetabolites, vitamin D and depigmentation agents.

For at least these reasons, Applicants submit that the presently claimed invention would not have been obvious over *Blank* in view of *Skotniki*. Accordingly, reconsideration and withdrawal of the rejection are in order.

As a final note, Applicants wish to point out that they have added claims 19-21 to further define preferred embodiments of the invention. Applicants submit that these claims are patentably distinguished from the cited references and combinations.

In particular, claims 19-21 are distinguished from the cited references because the claims define a composition comprising at least one active agent in combination with an amount of at least one TNF-alpha antagonist, at least one IL-1 antagonist and at least one TNF-alpha antagonist, and the at least one agent being selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts, anti-metabolites, vitamin D and depigmentation agents. As none of the cited references or combinations of references disclose or fairly suggest such compositions, Applicants submit that claims 19-21 are neither anticipated by nor rendered obvious by the cited references.

From the foregoing, Applicants earnestly solicit further and favorable action in the form of a Notice of Allowance.

If there are any questions concerning this paper or the application in general, the Examiner is invited to telephone the undersigned at his earliest convenience.

Respectfully submitted,

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Attachments: Terminal Disclaimer of U.S. Patent No. 6,060,061

Attachment to Amendment dated September 16, 2002

The invention relates to the use of a histamine antagonist, an interleukin-1 antagonist and/or a TNF-alpha antagonist in a cosmetic, pharmaceutical or dermatological composition for treating sensitive skins. It relates especially to the use of a histamine antagonist, an interleukin-1 antagonist and/or a TNF-alpha antagonist for preventing and/or combating skin irritations and/or sores and/or erythema and/or dysaesthesic sensations and/or sensations of inflammation [overheating] and/or pruritus and/or prickling and/or tingling and/or discomfort and/or tightness of the skin and/or mucosae. It also relates to a composition containing a histamine antagonist, an interleukin-1 antagonist and/or a TNF-alpha antagonist which limits or eliminates the irritant side-effects of certain products, and in particular of certain cosmetic, dermatological or pharmaceutical active agents.

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Paragraph number 7

The Applicants have carried out numerous clinical tests and have been able to determine the symptoms associated with sensitive skins. These symptoms are, in particular, subjective signs which are essentially dysaesthesic sensations. Dysaesthesic sensations are understood to mean more or less painful sensations experienced in an area of the skin, such as prickling, tingling, itching or pruritus, burning, inflammation, [overheating,] discomfort, tightness, and the like.--

Paragraph number 11

--An intolerant skin is a skin which reacts by sensations of inflammation [overheating] or of tightness, by pruritus, that is to say by itching or prickling, by tingling and/or red blotches, to different factors such as the environment, emotions and foods. In general, these signs are associated with erythema and with a skin with or without sores.

Paragraph number 12

"Sensitive" scalps have a more unequivocal symptomatology: the sensations of pruritus and/or of prickling and/or of inflammation [overheating] are essentially triggered by local factors such as rubbing, soap, surfactants, hard water with a high chalk concentration, shampoos or lotions. These sensations are also sometimes triggered by

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factors such as the environment, emotions and/or foods. Erythema and hyperseborrhoea of the scalp as well as a dandruff state are frequently associated with the above signs.

Paragraph number 13

Moreover, in some anatomical regions, such as the major folds (inguinal, genital, axillary, popliteal, anal and inframammary regions, bend of the elbow) and the feet, sensitive skin manifests itself in pruriginous sensations and/or dysaesthesic sensations (inflammation, [overheating,] prickling) associated especially with sweating, with rubbing, with wool, with surfactants, with hard water with a high chalk concentration and/or with temperature changes.

Paragraph number 20

In addition, the Applicants found that the addition of interleukin-1 antagonists and/or of TNF-alpha antagonists to cosmetic, pharmaceutical or dermatological compositions for topical application containing irritant products (alpha-hydroxy acids, retinoids, benzoyl peroxide, etc.) also enabled the irritation reactions usually caused by these products to be decreased or even eliminated. These irritation reactions manifest themselves within moments following application, in dysaesthesic sensations (inflammation, [overheating,] burning, itching or pruritus sensations, prickling sensations, tightness, etc.), and/or in red blotches, and/or in edema. These irritation states may also manifest

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themselves some time after application, in the persistence, appearance or reappearance of the above-mentioned dysaesthesic sensations and/or in red blotches and/or scales; these skin irritation states may assume the appearance of plaques of cutaneous xerosis and/or sores.

Paragraph number 24

The subject of the present invention is also the use in a topical composition of at least one compound chosen from interleukin-1 antagonists, TNF-alpha antagonists and combinations thereof, for preventing and/or combating skin irritations and/or sores and/or erythema and/or sensations of inflammation [overheating] and/or of dysaesthesia and/or pruritus and/or prickling and/or tingling and/or discomfort and/or tightness of the skin and/or mucosae.

Paragraph number 26

The subject of the present invention is also the use in a topical composition of at least one constituent chosen from histamine antagonists and combinations thereof, for preventing and/or combating skin irritations and/or sores and/or sensations of inflammation [overheating] and/or of dysaesthesia and/or prickling and/or tingling and/or discomfort and/or tightness of the skin and/or mucosae.

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1. (Amended) A composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising:

-- an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition,

-- an amount of at least one compound selected from the group consisting of interleukin-1 antagonists, TNF-alpha antagonists and combinations thereof, sufficient to prevent or alleviate said irritant side-effect, and a cosmetically, dermatologically or pharmaceutically acceptable medium therefor, wherein the agent which produces the irritant side-effect is selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D and depigmentation agents.

10. (Amended) A composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising

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an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition;

at least one compound selected from the group consisting of interleukin-1 antagonists, TNF alpha antagonists and combinations thereof, in an amount effective to antagonize said irritant side-effect;

and a cosmetically, dermatologically or pharmaceutically acceptable medium therefor, said compound being capable of inhibiting the IL-1-induced adhesion of macrophages to endothelial cells, inhibiting the IL-1-induced release of superoxide anions from neutrophils, inhibiting the TNF alpha-induced adhesion of macrophages to endothelial cells, inhibiting the TNF alpha-induced release of superoxide anions from neutrophils, inhibiting the mitogenic activity of TNF alpha by dermal fiproblasts, or inhibiting the release of interleukin-1 or TNF alpha by phorbol ester induced differentiated monocytes, and wherein the agent which produces an irritant side-effect is selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D, depigmentation agents.